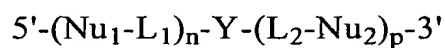


This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

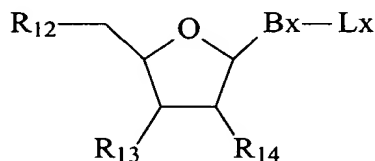
1- 22. (Cancelled).

23. (Currently Amended) An oligomeric compound of the formula:



wherein:

each Nu<sub>1</sub> and Nu<sub>2</sub>, independently, has the formula:



wherein

Bx is a heterocyclic base moiety;

Lx is hydrogen, a protecting group or a substituent group;

one of R<sub>12</sub>, R<sub>13</sub> and R<sub>14</sub> is hydroxyl, a protected hydroxyl, a covalent attachment to a solid support, a nucleoside, an oligonucleoside, a nucleotide, an oligonucleotide, a conjugate group or an optionally protected substituent group ;

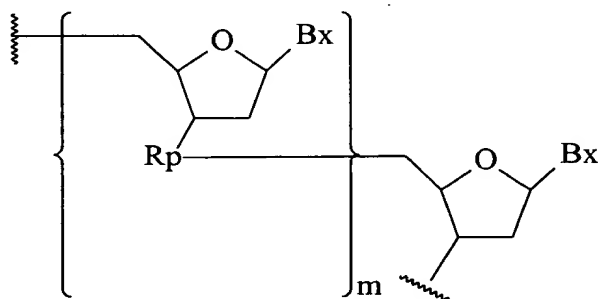
another of R<sub>12</sub>, R<sub>13</sub> and R<sub>14</sub> is hydrogen, hydroxyl, a protected hydroxyl or an optionally protected substituent group;

the remaining of R<sub>12</sub>, R<sub>13</sub> and R<sub>14</sub>, of Nu<sub>1</sub>, is L<sub>1</sub>;

the remaining of R<sub>12</sub>, R<sub>13</sub> and R<sub>14</sub>, of Nu<sub>2</sub>, is L<sub>2</sub>;

each  $L_1$  and each  $L_2$  is, independently, a phosphodiester, phosphorodithioate; chiral Sp phosphorothioate; phosphoramidate; thiophosphoramidate; phosphonate; methylene phosphonate; phosphotriesters; thionoalkylphosphonate; thionoalkylphosphotriester; borano-phosphate; boranothiophosphate; thiodiester; thionocarbamate; siloxane; carbamate; sulfamate; morpholino sulfamide; sulfonamide; sulfide; sulfonate; N,N'-dimethylhydrazine; thioformacetal; formacetal; thioketal; ketal; amine (-NH-CH<sub>2</sub>-CH<sub>2</sub>-); hydroxylamine; hydroxyimine; hydrazinyl; amide (-CH<sub>2</sub>-N(JJ)-C(O)-) and (-CH<sub>2</sub>-C(O)-N(JJ)-); oxime (-CH<sub>2</sub>-O-N=CH-); and alkylphosphorus (-C(JJ)<sub>2</sub>-P(=O)(OJJ)-C(JJ)<sub>2</sub>-C(JJ)<sub>2</sub>-), wherein each JJ is, independently, hydrogen or C<sub>1</sub> to C<sub>10</sub> alkyl wherein at least one of  $L_1$  and  $L_2$  is other than phosphodiester internucleoside linkage or a modified internucleoside linkage;

Y has the formula:



wherein:

each Rp is a chiral Rp phosphorothioate internucleotide linkage; and

each n, m and p is, independently, from 1 to 100; where the sum of n, m and p is from 3 to about 200;

~~with the proviso that at least one of  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$  and  $L_x$  is a substituent group or at least one of  $L_1$  and  $L_2$  is a modified internucleoside linkage;~~

wherein the oligomeric compound comprises from 5 to about 50 nucleosides.

24. (Original) The oligomeric compound of claim 23 wherein at least one Nu<sub>1</sub> or at least one Nu<sub>2</sub> comprises a substituent group.

25. (Original) The oligomeric compound of claim 24 wherein at least one Nu<sub>1</sub> and at least one Nu<sub>2</sub> independently comprise a substituent group.

26. (Original) The oligomeric compound of claim 23 wherein each Nu<sub>1</sub> and each Nu<sub>2</sub> independently comprises a substituent group.

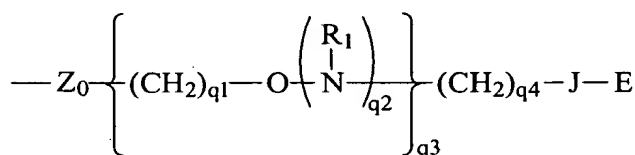
27. (Original) The oligomeric compound of claim 24 wherein said substituent group is covalently attached to the 2', 3' or 5'-position of said Nu<sub>1</sub> or Nu<sub>2</sub>.

28. (Original) The oligomeric compound of claim 27 wherein said substituent group is covalently attached to the 2'-position of said Nu<sub>1</sub> or Nu<sub>2</sub>.

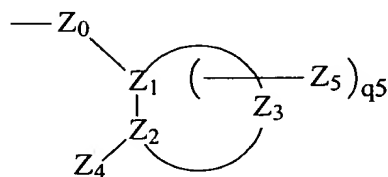
29. (Original) The oligomeric compound of claim 23 wherein each of said substituent groups is, independently, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>5</sub>-C<sub>20</sub> aryl, O-alkyl, O-alkenyl, O-alkynyl, O-alkylamino, O-alkylalkoxy, O-alkylaminoalkyl, O-alkyl imidazole, thiol, S-alkyl, S-alkenyl, S-alkynyl, NH-alkyl, NH-alkenyl, NH-alkynyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, N-phthalimido, halogen keto, carboxyl, nitro, nitroso,

nitrile, trifluoromethyl, trifluoromethoxy, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, heterocycle, carbocycle, polyamine, polyamide, polyalkylene glycol, and polyether;

or each substituent group has one of formula I or II:



I



II

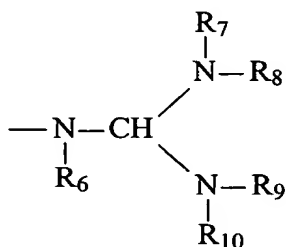
wherein:

Z<sub>0</sub> is O, S or NH;

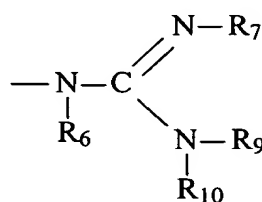
J is a single bond, O or C(=O);

E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(R<sub>1</sub>)(R<sub>2</sub>), N(R<sub>1</sub>)(R<sub>5</sub>), N=C(R<sub>1</sub>)(R<sub>2</sub>), N=C(R<sub>1</sub>)(R<sub>5</sub>) or has one of formula

III or IV;



III



IV

each R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub> and R<sub>10</sub> is, independently, hydrogen, C(O)R<sub>11</sub>, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or

unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally, R<sub>7</sub> and R<sub>8</sub>, together form a phthalimido moiety with the nitrogen atom to which they are attached;

or optionally, R<sub>9</sub> and R<sub>10</sub>, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R<sub>11</sub> is, independently, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, trifluoromethyl, cyanoethyloxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

R<sub>5</sub> is T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a solid support material;

each R<sub>1</sub> and R<sub>2</sub> is, independently, H, a nitrogen protecting group, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, wherein said substitution is OR<sub>3</sub>, SR<sub>3</sub>, NH<sub>3</sub><sup>+</sup>, N(R<sub>3</sub>)(R<sub>4</sub>), guanidino or acyl where said acyl is an acid amide or an ester;

or R<sub>1</sub> and R<sub>2</sub>, together, are a nitrogen protecting group or are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

or R<sub>1</sub>, T and L, together, are a chemical functional group;

each R<sub>3</sub> and R<sub>4</sub> is, independently, H, C<sub>1</sub>-C<sub>10</sub> alkyl, a nitrogen protecting group, or R<sub>3</sub> and R<sub>4</sub>, together, are a nitrogen protecting group;

or  $R_3$  and  $R_4$  are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

$Z_4$  is OX, SX, or  $N(X)_2$ ;

each X is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)R_5$ ,  $C(=O)N(H)R_5$ , or  $OC(=O)N(H)R_5$ ;

$R_5$  is H or  $C_1$ - $C_8$  alkyl;

$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(R_1)(R_2)$  OR<sub>1</sub>, halo, SR<sub>1</sub> or CN;

each  $q_1$  is, independently, an integer from 1 to 10;

each  $q_2$  is, independently, 0 or 1;

$q_3$  is 0 or an integer from 1 to 10;

$q_4$  is an integer from 1 to 10;

$q_5$  is from 0, 1 or 2; and

provided that when  $q_3$  is 0,  $q_4$  is greater than 1.

30. (Cancelled).

31. (Original) The oligomeric compound of claim 30 wherein at least one of  $L_1$  and at least one of  $L_2$  is a modified internucleoside linkage.

32-33. (Cancelled).

34. (Original) The oligomeric compound of claim 30 wherein each modified internucleoside linkage is, independently, methyl phosphonate, boranophosphonate, phosphoramidate, 3'-methylenephosphonate or methylene(methyylimino).

35. (Original) The oligomeric compound of claim 23 wherein at least one  $R_{14}$  is  $L_1$  or  $L_2$ .

36. (Original) The oligomeric compound of claim 23 wherein at least one  $R_{14}$  is  $L_1$  and at least one  $R_{14}$  is  $L_2$ .

37. (Cancelled).

38. (Original) The oligomeric compound of claim 23 comprising from 8 to about 30 nucleosides.

39. (Original) The oligomeric compound of claim 23 comprising from 15 to about 25 nucleosides.

**DOCKET NO.: ISIS-4288**  
**Application No.: 09/438,989**  
**Office Action Dated: September 10, 2003**

**PATENT**  
**REPLY FILED UNDER EXPEDITED**  
**PROCEDURE PURSUANT TO**  
**37 CFR § 1.116**

40 - 44. (Cancelled).